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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/667,111 | 09/17/2003 | Patrick Bernardelli | PC25382A | 9341 |
| 28523 | 7590 | 03/15/2005 | | EXAMINER |
| PFIZER INC. PATENT DEPARTMENT, MS8260-1611 EASTERN POINT ROAD GROTON, CT 06340 | | | TRUONG, TAMTHOM NGO | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1624 | |

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/667,111 | BERNARDELLI ET AL. | |
| | Examiner | Art Unit | |
| | Tamthom N. Truong | 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) Claim(s) ____ is/are allowed.
- 6) Claim(s) 1-17 is/are rejected.
- 7) Claim(s) ____ is/are objected to.
- 8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. ____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>9-17-03</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: ____ . |

DETAILED ACTION

Claims 1-17 are pending.

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. Claim 1 recites the limitation of (C₁-C₆)alkyl which is substituted with the following substituents:

OC(=O)R⁷ (i.e., OR⁴ with R⁴ a C(=O)R⁷); or

NR⁵-SO₂R⁶ (i.e., NR⁴R⁵ with R⁴ as SO₂R⁶); or

NR⁵-SO₂NR⁷R⁸ (i.e., NR⁴R⁵ with R⁴ as SO₂NR⁷R⁸) or

NR⁵-C(=O)NR⁷R⁸ (i.e., NR⁴R⁵ with R⁴ as C(=O)NR⁷R⁸).

However, the same alkyl group can also be substituted with the following groups:

OC(=O)R^{4a}; or

NR-SO₂-R³; or

NR-SO₂-NR^{4a}R^{5a}; or

NR-C(=O)- NR^{4a}R^{5a}

The scopes of R³, R^{4a}, R^{5a} are broader than the scopes of R⁵-R⁸. Therefore, it is unclear as to which set of substituents on the alkyl group is intended (i.e., one with broader scope or one with narrower scope).

b. Claim 1 recites the phrase "*pharmaceutically acceptable derivative thereof*" which has indefinite metes and bounds because the specification provides such an open-ended description, and thus, it is not clear what other compounds would constitute a "*derivative thereof*" besides solvates, hydrates, and salts.

c. Claim 11 recites species. However, it is unclear if each species is claimed, or a mixture of some (or all) species is claimed.

d. Claims 2-10 and 12-17 are rejected as being dependent on claim 1, and carrying over limitations that are indefinite.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 12-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of AIDS (or HIV infection), does not reasonably provide enablement for the treatment of other diseases such as: *T-cell related diseases, autoimmune diseases, osteoarthritis, rheumatoid arthritis, multiple sclerosis, osteoporosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, leukemia, allergy, inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, pancreatitis, dermatoses, psoriasis, atopic dermatitis, glomerulonephritis, conjunctivitis, autoimmune diabetes, graft rejection, epilepsy, muscular atrophy and systemic lupus erythematosus.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 12 recites a “*method of treating a disease for which PDE7 inhibition therapy is indicated in a mammal...*” which covers an array of diseases as recited in claims 13-16.

Claim 13 depends on claim 12, and recites specific diseases such as: *T-cell related diseases, autoimmune diseases, osteoarthritis, rheumatoid arthritis, multiple sclerosis, osteoporosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, leukemia, acquired immune deficiency syndrome (AIDS), allergy, inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, pancreatitis, dermatoses, psoriasis, atopic dermatitis, glomerulonephritis, conjunctivitis, autoimmune diabetes, graft rejection, epilepsy, muscular atrophy and systemic lupus erythematosus.*

Claim 14 depends on claim 13, but only recites *asthma, allergy or atopic dermatitis.*

Claim 15 depends on claim 13, but only recites *osteoporosis.*

Claim 16 depends on claim 13, but only recites *cancer.*

Thus, together, the scope of claims 12-16 covers the treatments of many diseases that affect different organs or systems such as: bones, joints, immune system, lungs, eyes, skin, neurological system, colon, stomach, pancreas, etc. All of the cited diseases have different underlying factors. The treatment of one might even be contraindicated in the other.

The amount of direction or guidance presented: The specification only provides a reference for the *in-vitro* assay of the inhibition of PDE7. Compounds #1-6 were disclosed to

have IC₅₀ of less than 1 μM, which is much too general for an IC₅₀. The specification does not show evidences for the treatments of the following diseases:

- i. No evidence shown for an effect on T-cell to treat T-cell mediated diseases.
- ii. No evidence shown for an increased bone density to treat osteoporosis.
- iii. No evidence shown for an increased motion range to treat osteoarthritis or rheumatoid arthritis.
- iv. No evidence shown for the inhibition of mitosis to treat cancer.
- v. No evidence shown for an increased production of erythrocytes to treat leukemia.
- vi. No evidence shown for bronchodilation to treat COPD or asthma.
- vii. No correlation shown between PDE7 inhibition and the treatment of allergy, inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, pancreatitis, dermatoses, psoriasis, atopic dermatitis, glomerulonephritis, conjunctivitis, autoimmune diabetes, graft rejection, epilepsy, muscular atrophy and systemic lupus erythematosus.

In short, the specification does not provide sufficient guidance for the skilled clinician to use the claimed compounds in the treatment of many diseases that are allegedly related to the inhibition of PDE7.

The state of the prior art: As evidence by the reference of Bricher et. al. (EP 530,994 A1), the spiro-quinazolinone compounds are disclosed as a possible permutation that can inhibit HIV reverse transcriptase. Thus, following such a teaching, at best, the skilled clinician could only use the claimed compounds in the treatment of AIDS.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in undue experimentation to establish data that would adequately support the use of the claimed compounds in the treatment of *T-cell related diseases, autoimmune diseases, osteoarthritis, rheumatoid arthritis, multiple sclerosis, osteoporosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, leukemia, acquired immune deficiency syndrome (AIDS), allergy, inflammatory bowel disease (IBD), ulcerative colitis, Crohn's disease, pancreatitis, dermatoses, psoriasis, atopic dermatitis, glomerulonephritis, conjunctivitis, autoimmune diabetes, graft rejection, epilepsy, muscular atrophy and systemic lupus erythematosus.*

Such a task would require a tremendous amount of effort, time and resources.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only discloses that the claimed compounds have IC₅₀ of less than 1 μM. However, said evidence does not adequately guide the skilled clinician in the treatment of diseases that would require the treatment of other underlying factors that are not related to PDE7. Thus, with such a limited teaching, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the methods recited in claims 12-16.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-26 of copending Application No. 10/852,404 (or US 2004/0214843 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant formula (I) overlaps with the formula (I) of the copending application when variables of the copending application have the following meanings:

- i. X_1-X_4 are independently $-C(R^1)-$; wherein R^1 is alkyl (which corresponds to the instant R^1), or R^1 is X^5R^5 (which corresponds to the instant $-OR^2$);
- ii. Y is NR^{12} wherein R^{12} is hydrogen;
- iii. A is a ring of 4-, 5- or 7-membered ring with ring atoms of A^1 , and/or A^2 , A^4 , A^5 ;
- iv. Z is O.

Claim 1 of the copending application differs from the instant claim 1 by having a broader scope and reciting formulae II and III. However, regarding formula I, there is substantial overlapping subject matter as listed above. Furthermore, two species in claims 22 and 23 of the copending applications (see US 2004/0214843 A1, page 66, left column, lines 49 and 52; also page 67, right column, lines 10 and 13) read on the instant formula (I).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

References cited on PTO-892

Besides EP 530,994, which is cited for enablement, all other references are cited for state of the art which shows the possibility of a spiro-quinazolinone compound. However, because they fail to teach a substituent corresponding to the instant OR², they do not anticipate the instant formula I. Also, there is no nexus between them and EP'994 for a prima facie case of obviousness.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

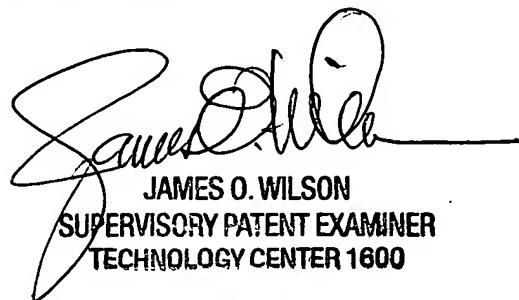
Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



*Tamthom N. Truong
Examiner
Art Unit 1624*

2-25-05



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